Original Article
MVP Journal of Medical Sciences, *Vol 8(2), 183-190, July-December 2021*
ISSN (Print) : 2348–263X
ISSN (Online) : 2348-2648
DOI: 10.18311/mvpjms/2021/v8i2/321

Comparison of Intubating Conditions in Patients Induced with Succinylcholine, Atracurium and Priming with Atracurium

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Abstract

Background: This was a comparative observational study to compare the intubating conditions in patients posted for elective surgeries under general anaesthesia using succinylcholine, atracurium or priming with atracurium. Depolarizing muscle relaxant, frequently used for rapid sequence endotracheal intubation, has serious complications that occur intermittently, such as, hyperkalemia, increased intraoccular pressure and sudden cardiac arrest. So the priming principle, i.e., the administration of a subparalyzing dose of a nondepolarizing muscle relaxant (priming dose) prior to the intubating dose, was developed for rapid sequence endotracheal intubation with nondepolarizing muscle relaxant. This study compares the intubating conditions using a depolarizing muscle relaxant, a nondepolarizing muscle relaxant and priming with a nondepolarizing muscle relaxant. **Methodology:** Total 114 patients scheduled for elective surgeries were allocated into 3 groups. We assessed the intubating conditions with jaw relaxation, position of vocal cords, response to intubation (coughing, straining or muscular movements), haemodynamic response to intubation and number and strength of twitches to train of four stimuli just before intubation. **Results:** All the patients in different study groups were comparable in terms of age, sex, ASA status. The mean SBP, DBP was statistically significantly higher in Group B as compared to Group C group and Group A from 1 minute after intubation till after extubation. Good jaw relaxation was most commonly observed in group A (100%) as compared to group C (31%) and group B (17.5%) and the difference was statistically significant. Open vocal cord was most commonly observed in group A (100%) as compared to group C (75%) and group B (23%) and the difference was statistically significant. Severe coughing was most commonly observed in group B (17.5%) as compared to group C (0%) and group A (0%) and the difference was statistically significant. Severe muscular movements was most commonly observed in group B (21%) as compared to group C (0%) and group A (0%) and the difference was statistically significant.1,2,3 twitch was most commonly observed in group B (100%) as compared to group C (77.5%) and group A (56%) and the difference was statistically significant. Increase in BP and pulse > 20% of basal values was most commonly observed in group B (42%) as compared to group C (0%) and group A (0%) and the difference was statistically significant. Excellent to good scoring was most commonly observed in group A (100%) as compared to group C (92.5%) and group B (25%) and the difference was statistically significant. **Conclusion:** Succinylcholine is still the ideal choice for rapid sequence induction. Priming with atracurium can be used as an efficient alternative when succinylcholine is contraindicated.

Keywords: Succinylcholine, Atracurium, Intubation, Muscle Relaxant, Elective Surgery

1. Introduction

Atracurium is a benzyl-isoquinolinium diester, non-depolarizing neuromuscular blocking agent of intermediate duration of action[1,2]. Its lack of significant cardiovascular effects and its lack of dependence on good kidney function for elimination provide clinical advantage over alternate non-depolarizing neuro muscular blocking agents.

One of the main differences between the depolarizing and the non-depolarizing muscle relaxant is the on set

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time[3]. Suxamethonium can produce profound muscle relaxation suitable for endo-tracheal intubation from 45 seconds where as the non-depolarizing muscle relaxants requires two minutes or more to produce adequate relaxation for intubation. When atracurium is used fore ndotracheal intubation, intubation cannot be accomplished satisfactorily, which prevents its routine use, whenever rapid intubation is desired[4]. Speed of onset of neuromuscular block is one of the requirements to rapidly secure the airway and this is consistently provided by succinylcholine within 60–90 seconds, but its use has serious complications that occur occasionally, such as hyperkalemia, increased intra ocular pressure, sudden cardiac arrest especially in infants and adolescents[5,6].

In order to facilitate rapid endotracheal intubation with non-depolarising agents, priming principle has been used in the recentpast[7,8].

The priming principle refers to the administration of a small (subparalysing) dose of non- depolarizing neuromuscular blocking drug a few minutes before the intubating dose is given. The rationale is based on the fact that the high margin of safety of neuromuscular transmission allows 70-75% occupancy of cholinergic receptors without any significant effect on neuro-muscular activity. The administration of a second larger dose at the time of development of maximal effect of priming dose rapidly increases receptor occupancy to over 90% required for profound neuromuscular blockade[9]. It was suggested the priming dose be 15-20% of the customary in tubating dose and priming time interval be 3-4 min. However priming carries risk of aspiration, difficulty in swallowing and the visual disturbances, which even in subtle degree may be uncomfortable for the patient[10,11].

There we conducted this study in order to compare the intubating conditions in patients induced with succinylcholine, atracurium and priming with atracurium at a tertiary care centre.

2. Aims and Objectives

- To compare jaw relaxation and position of vocal cords amongst patients induced with succinylcholine, atracurium and priming with atracurium.
- To compare response to intubation amongst patients induced with succinylcholine, atracurium and priming with atracurium.
- To compare haemodynamic response amongst patients induced with succinylcholine, atracurium and priming with atracurium.

3. Materials and Methods

This comparative observational study (longitudinal) was conducted on 114 adult patients posted for elective surgeries under general anaesthesia at at Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik, Maharashtra.

Duration of Study: August 2018 to December 2020.

3.1 Inclusion Criteria

- All Patients scheduled for elective surgeries under general anaesthesia.
- American Society of Anesthesiologists Classification I and II patients.
- Age group 18-60 years.

3.2 Exclusion Criteria

- Patient refusal to participate in the study.
- Anticipated Difficult intubation.
- Mouth opening < 2.5 cm
- BMI > 35 kg/m^2
- Patients with cardiorespiratory system compromise.
- Pregnancy.
- Patients with neuromuscular disease.
- Documented allergic reaction to the anaesthetic agent being used.
- Emergency surgeries.

3.3 Statistical Analysis

All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 22 for analysis. Qualitative data was presented as frequency and percentages and analysed using chi-square test. Quantitative data was presented as mean and SD and compared using ANOVA test. P-value < 0.05 was taken as level of significance.

4. Observations and Results

Group A - Patients receiving succinylcholine 2 mg/kg and intubation at 90 seconds after single dose.

Group B - Patients receiving single intubating dose of 0.5 mg/kg atracurium and intubation as soon as relaxation is achieved.

Group C - Patients receiving priming dose with 0.08 mg/kg atracurium and intubation after second dose of atracurium 0.42 mg/kg.

Data are presented in Mean ± /SD or absolute numbers. P value <0.05 is statistically significant

The mean age of patients in Groups A, Group B and Group C was 37.69 ± 14.91 years, 41.50 ± 10.65 years and 40.23 ± 14.23 years respectively. Statistically, there was no significant difference among the groups (p = 0.585). The mean weight of patients in Groups A, Group B and Group C was 65.19 ± 6.08 kg, 66.73 ± 7.6 and 66.43 ± 6.1 kg respectively. Statistically, there was no significant difference among the groups (p = 0.218). The mean height of patients in Groups A, Group B and Group C was 164.71 ± 8.7 cm, 163.12 ± 7.6 cm and 160.14 ± 5.2 cm respectively. Statistically, there was no significant difference among the groups (p = 0.923). The gender ratio (M:F) in Group A was 22/16, Group B was 24/14, Group C was 23/15, these are comparable as P value is 0.648. Statistically, there was no significant difference among the groups (p = 0.648). ASA Physical Status Ratio (I/II) was 20/18 in Group C, 22/16 in Group A, 21/17 in Group B Both groups did not differ significantly in their ASA Physical status. (P value = 0.076) (Table 1).

Table 1. Demographic profile amongst study population

	Group A	Group B	Group C	P value
Age (years)	37.69 ± 14.91	41.50 ± 10.65	40.23 ± 14.23	0.585
Weight (kg)	65.19 ± 6.08	66.73 ± 7.6	66.43 ± 6.1	0.218
Gender (M/F)	22/16	24/14	23/15	0.648
ASA (I/II)	20/18	22/16	21/17	0.076
Height	164.71 ± 8.7	163.12 ± 7.6	159.14 ± 5.2	0.923

Table 2. Changes in heart rate at various intervals amongst different study population

Heart Rate	Group A		Group B		Group C		P value
	Mean	SD	Mean	SD	Mean	SD	
One day prior	84.98	5.5	85.4	6.9	84.87	6	0.928
Before induction	82.65	5.4	83.4	6.3	83.87	5.6	0.563
At the time of induction	83.93	5.6	84.93	6.7	84.53	5.9	0.815
1 min after induction	80.43	5.3	92.27	6.7	88.33	5.8	0.001
5 mins after induction	79.13	5.2	91.93	6.8	87.07	6	0.001
15 mins after induction	75.6	4.8	89.2	5.9	84.2	5.9	0.001
After extubation	74.2	3.4	87.8	4.5	82.8	4.5	0.001

Table 3. Changes in SBP at various intervals amongst different study population

SBP	Group A		Group B		Group C		P value
	Mean	SD	Mean	SD	Mean	SD	
One day prior	127.9	11.4	126.6	10	126.3	9.4	0.803
Before induction	125.5	10.1	124.5	9.9	125.7	8.1	0
At the time of induction	126.5	10.3	125.5	9.9	124.7	8.5	0.768
1 min after induction	125.2	9.5	131.1	7.6	127.2	8.7	0.001
5 mins after induction	122.2	7.2	132.3	7.9	125.9	8	0.001
15 mins after induction	120.4	6.2	129.9	5.8	124.7	5.7	0.001
After extubation	119	4.8	128.5	4.4	123.3	4.3	0.001

At baseline all the three groups were comparable and there was no statistically significant difference among the groups (p = 0.928). The mean heart rate was statistically significantly higher in Group B as compared to Group C group and Group A from 1 minute after intubation till after extubation (Table 2).

At baseline all the three groups were comparable and there was no statistically significant difference among the groups (p = 0.803). The mean SBP was statistically significantly higher in Group B as compared to Group C group and Group A from 1 minute after intubation till after extubation (Table 3).

At baseline all the three groups were comparable and there was no statistically significant difference among the groups (p = 0.211). The mean DBP was statistically significantly higher in Group B as compared to Group C group and Group A from 1 minute after intubation till after extubation (Table 4).

At baseline all the three groups were comparable and there was no statistically significant difference in SpO_2 among the groups at various interval (Table 5).

As seen in the (Table 6), good jaw relaxation was most commonly observed in group A (100%) as compared to group C (31%) and group B (17.5%) and the difference was statistically significant.

As seen in (Table 7), Open vocal cord was most commonly observed in group A (100%) as compared to group C (75%) and group B (23%) and the difference was statistically significant.

Table 4. Changes in DBP at various intervals amongst different study population

DBP	Group A		Group B		Group C		P value
	Mean	SD	Mean	SD	Mean	SD	
One day prior	79.87	4.4	81.6	3	80.2	4.4	0.211
Before induction	77.67	3.6	78.33	3.8	78.53	3.9	0.498
At the time of induction	78.67	3.8	79.33	4	79.53	4	0.677
1 min after induction	77.73	3.8	84.8	3.2	78.13	3.2	0.001
5 mins after induction	74.2	2.8	83.53	2.8	77.4	2.8	0.001
15 mins after induction	72.93	2	81.07	2.9	74.8	2.8	0.001
After extubation	71.53	0.6	79.67	1.5	73.4	1.4	0.001

Table 5. Changes in SpO_2 at various intervals amongst different study population

SpO_2	Group A		Group B		Group C		P value
	Mean	SD	Mean	SD	Mean	SD	
One day prior	99.13	0.973	99.03	0.928	98.97	0.865	0.782
Before induction	98.9	0.351	99.19	0.4	98.93	0.1	0.743
At the time of induction	99.93	0.254	100	0	99.93	0.254	0.359
1 min after induction	99.97	0.183	99.93	0.254	99.93	0.365	0.866
5 mins after induction	99.93	0.254	99.87	0.434	99.97	0.183	0.446
15 mins after induction	99.93	0.54	100	0	99.93	0.254	0.359
After extubation	98.53	0.78	98.6	0.92	98.53	0.78	0.998

Table 6. Jaw relaxation

Jaw relaxation	Group A	Group B	Group C	P value
Poor	0 (0%)	1 (2.5%)	0 (0%)	0.001
Moderate	0 (0%)	30 (80%)	26 (69%)	
Good	38 (100%)	7 (17.5%)	12 (31%)	
Total	38 (100%)	38 (100%)	38 (100%)	

As seen in (Table 8), severe coughing was most commonly observed in group B (17.5%) as compared to group C (0%) and group A (0%) and the difference was statistically significant.

As seen in the (Table 9), severe muscular movements was most commonly observed in group B (21%) as compared to group C (0%) and group A (0%) and the difference was statistically significant.

As seen in (Table 10), twitch was most commonly observed in group B (100%) as compared to group C (77.5%) and group A (56%) and the difference was statistically significant.

Table 7. Position of vocal cord

Position of vocal cord	Group A	Group B	Group C	P value
Closed	0 (0%)	6 (16%)	2 (4%)	0.01
Semiclosed	0 (0%)	23 (61%)	8 (21%)	
Open	38 (100%)	9 (23%)	29 (75%)	
Total	38 (100%)	38 (100%)	38 (100%)	

Table 8. Response to intubation – Coughing

Coughing	Group A	Group B	Group C	P value
Severe	0 (0%)	7 (17.5%)	0 (0%)	0.001
Mild	2 (4%)	22 (59%)	3 (59%)	
No	36 (96%)	9 (23.5%)	35 (23.5%)	
Total	38 (100%)	38 (100%)	38 (100%)	

Table 9. Response to intubation - Muscular movements

Muscular movements	Group A	Group B	Group C	P value
Severe	0 (0%)	8 (21%)	0 (0%)	0.001
Mild	3 (8%)	29 (76%)	4 (11%)	
No	35 (92%)	1 (3%)	34 (89%)	
Total	38 (100%)	38 (100%)	38 (100%)	

Table 10. Number and strength of switches on TOF

No and strength of switches on TOF	Group A	Group B	Group C	P value
1,2,3 twitch	21 (56%)	38 (100%)	29 (77.5%)	0.001
1,2 twitch	17 (44%)	0 (0%)	9 (22.5%)	
1 twitch	0 (0%)	0 (0%)	0 (0%)	
Total	38 (100%)	38 (100%)	38 (100%)	

Table 11. Rise in BP and pulse

Rise in BP and Pulse	Group A	Group B	Group C	P value
Increase in BP and pulse > 20% of basal values	0 (0%)	16 (42%)	0 (0%)	0.001
Increase in BP and pulse 10- 20% of basal values	16 (43%)	22 (58%)	29 (77%)	
Increase in BP and pulse < 10% of basal values	22 (57%)	0 (0%)	9 (23%)	
Total	38 (100%)	38 (100%)	38 (100%)	

Table 12. Scoring system amongst different study population

Scoring system	Group A	Group B	Group C	P value
Excellent	25 (65%)	0 (0%)	4 (10%)	0.001
Good	13 (35%)	10 (25%)	31 (82.5%)	
Fair	0 (0%)	20 (52.5%)	3 (7.5%)	
Poor	0 (0%)	9 (22.5%)	0 (0%)	
Total	38 (100%)	38 (100%)	38 (100%)	

As seen in (Table 11), increase in BP and pulse >20% of basal values was most commonly observed in group B (42%) as compared to group C (0%) and group A (0%) and the difference was statistically significant.

As seen in (Table 12), excellent to good scoring was most commonly observed in group A (100%) as compared to group C (92.5%) and group B (25%) and the difference was statistically significant.

5. Discussion

The introduction of neuromuscular blockers revolutionized the anesthetic practice, which thereafter underwent a conceptual change. Muscle relaxants are classified into two groups, the depolarizers and nondepolarisers. Suxamethonium is the only depolarizer in use which causes profound muscle relaxation within 60 seconds after intravenous administration. Important nondepolarisers in clinical use in our country are vecuronium, atracurium, cisatracurium and rocuronium. They cause competitive blockade of neuromuscular junction. Most of the nondepolarisers have slower onset of action and are not suitable for rapid control of airway. In 1956, Stenlake, et al. synthesized atracurium. Atracurium and its isomers are different from other nondepolarisers because of their organ independent elimination. Atracurium is eliminated predominantly by two pathways: Ester hydrolysis and Hofmann elimination[12,13]. Suxamethonium remains the drug of choice when rapid tracheal intubation is needed. However, there are certain clinical situations wherein suxamethonium is contraindicated[14]. Hence, efforts were made to hasten the onset of action of nondepolarisers. These include priming technique, or the use of high doses of an individual agent or by a combination of different neuromuscular blockers[6]. With higher dose of atracurium (0.6 mg/kg), onset of action is faster and produced improved conditions for intubation. Higher doses also caused more adverse reactions such as cutaneous flushing, hypotension and bronchospasm due to histamine release[15].

The priming principle was introduced in 1980s to decrease the time of onset of action of NDMR. With the use of rocuronium this method is somewhat forgotten, although still used. In this method a small, subparalyzing dose of the nondepolarizing agent (20% of the ED_{95} or 10% of the intubating dose) is administered to the patient 2–4 min before the intubating dose of the drug. The mechanism is that when priming dose is administered, it will accelerate the onset of neuromuscular blockade by 30–60 s, thereby facilitating intubation quickly within 90 s after the intubating dose[6], Priming dose results in 70%–75% of cholinergic receptor occupancy and subsequent dose administered after the priming dose leads to >90% receptor occupancy, which is required for profound muscle relaxation. In reality, intubating conditions after priming do not match those after suxamethonium. Some adverse effects were also encountered while priming had been employed and these are patient discomfort, aspiration risks, difficulty in swallowing/coughing and diplopia[6,11]. This technique is not applicable for those with difficult airway and increased sensitivity to neuromuscular blocking drugs such as myasthenia gravis or those who are taking drugs known to interfere with neuromuscular function.

All the patients in different study groups were comparable in terms of age, sex, ASA status.

In the present study, the mean SBP, DBP was statistically significantly higher in Group B as compared to Group C group and Group A from 1 minute after intubation till after extubation. This findings was comparable with the study conducted by MISHRA et al., in which In group C 47.5% (19) had less than 10% increase and 50% (2) had 10-20% increase in MAP whereas in group A, 25% (10) has less than 10% increase, 50% (20) had 10-20% increase and 25% (10) showed more than 20% increase. In group B, 47.5% (19) and 45% (18) showed more than 20% and

between 10-20% increase respectively. Group D showed rise of more than 20% in 25% (10) patients, between 10-20% rise in 40% (20) patients and less than 10% rise in 25% (10) patients. There was a statistically significant difference between the groups[16].

In the present study, excellent to good scoring was most commonly observed in group A (87%) as compared to group C (79%) and group B (66%) and the difference was statistically significant. In a study conducted by Mishra et al. on the effect of priming on intubating conditions produced by atracurium, they found that atracurium in a total dose of 0.7 mg/kg utilizing priming principle provided excellent intubating conditions at 120s after intubating dose[16]. Priming dose of 0.1 mg/kg (i.e., approximately 14.3% of total dose) appeared satisfactory without any side effects[20].

In the present study, good jaw relaxation was most commonly observed in group A (100%) as compared to group C (31%) and group B (17.5%) and the difference was statistically significant. This findings was comparable with the study conducted by MISHRA et al., in which In group C 100% (40) patients had good relaxation, whereas only 47.50% (19) had good and 50% (20) has moderate jaw relaxation among group A patients. Group B showed only 20% (8) to have good and 75% (30) to have moderate jaw relaxation. In group D 90% (36) had good and 10% (4) had moderate jaw relaxation. There was statistically a significant difference between the groups.[20]

In the present study, Open vocal cord was most commonly observed in group A (100%) as compared to group C (75%) and group B (23%) and the difference was statistically significant. This findings was comparable with the study conducted by MISHRA et al., in which groups C 100% (40) patients had open vocal cords, whereas group A had 72.5% (29) open, 25% (10) semi closed and 2.5% (1) closed vocal cords. In group B 22.5% (9) had open, 67.5% (27) semi closed and remaining 10% (4) had closed vocal cords. In group D, 80% (32) had open and 20% (8) semi closed vocal cords. There was a statistically significant difference between the groups[16].

In the present study, severe coughing was most commonly observed in group B (17.5%) as compared to group C (0%) and group A (0%) and the difference was statistically significant. This findings was comparable with the study conducted by MISHRA et al., in which both groups A and C, 95% (38 had nil incidence of coughing/straining, whereas in groups has B only 32.5% (13) had nil and 45% (18) had moderate incidence. In group D 57.5% (23) had nil and 40% (16) had moderate incidence of coughing/straining in response to intubation[16].

In the present study, severe muscular movements was most commonly observed in group B (21%) as compared to group C (0%) and group A (0%) and the difference was statistically significant.

In the present study, 1,2,3 twitch was most commonly observed in group B (100%) as compared to group C (77.5%) and group A (56%) and the difference was statistically significant.

In the present study, Increase in BP and pulse >20% of basal values was most commonly observed in group B (42%) as compared to group C (0%) and group A (0%) and the difference was statistically significant.

In 1986, Naguib et al. conducted a study to find out the optimal priming dose of atracurium using wider range of priming dose of atracurium (from 0.04 mg/kg to 0.09 mg/kg) with a priming interval of 3 min. In this study, priming doses in the range of 0.04–0.09 mg/kg were associated with statistically significant reduction in the TOF ratios, which facilitated rapid tracheal intubation. The optimal priming dose of atracurium was 0.05 mg/kg, which had lesser incidence of adverse effects related to priming. They concluded that optimal priming dose of atracurium was 0.05 mg/kg, which has lesser incidence of adverse effects related to priming[17]. In our study, we used a priming dose of 0.08 mg/kg body weight 3 min before intubating dose, which had further helped to reduce the incidence of adverse effects. In our study, time after intubating dose required for TOF count to reach zero was far higher than ideal time of <90 s required for rapid sequence intubation.

Another study conducted by Naguib et al. regarding rapid tracheal intubation with atracurium and comparing the priming intervals concluded that when priming dose of atracurium is given 3 min before the intubating dose, it can prove as an alternative to succinylcholine for rapid endotracheal intubation[18]. In our study, we have used a priming interval of 3 min, which is optimal as found out by several other studies. In a study conducted by Mishra et al. on the effect of priming on intubating conditions produced by atracurium, they found that atracurium in a total dose of 0.7 mg/kg utilizing priming principle provided excellent intubating conditions at 120 s after intubating dose. Priming dose of 0.1 mg/kg (i.e., approximately 14.3% of total dose) appeared satisfactory without any side effects[16].

7. Conclusion

Atracurium in a total dose of 0.5 mg/kg for intubation, utilizing priming principle, provided excellent intubating conditions at 120 seconds after the intubating dose. A priming dose of 0.08 mg/kg (i.e. approximately 14.3% of total dose) appeared satisfactory and devoid of any untoward effects. Succinylcholine is still the ideal choice for rapid sequence induction. Priming with atracurium can be used as an efficient alternative when succinylcholine is contraindicated.

8. References

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How to cite this article: Phulkar, S., Parikh, RY and Pawar, H. Comparison of Intubating Conditions in Patients Induced with Succinylcholine, Atracurium and Priming with Atracurium. MVP J. Med. Sci. 2020; 8(2): 183-190.